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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/560,470	12/14/2005	Deborah A. Lannigan-Macara	00910-05	5125

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UNIVERSITY OF VIRGINIA PATENT FOUNDATION
250 WEST MAIN STREET, SUITE 300
CHARLOTTESVILLE, VA 22902

EXAMINER	
HARRIS, ALANA M	
ART UNIT	**PAPER NUMBER**
1643	

MAIL DATE	DELIVERY MODE
01/17/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/560,470	LANNIGAN-MACARA ET AL.	
	Examiner	Art Unit	
	Alana M. Harris, Ph.D.	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *1-14,19 and 20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *03/16/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group IV (claims 15-18) in the reply filed on October 31, 2007 is acknowledged. The traversal is on the ground(s) that "[it] should be recombined with Group IV" and "the PCT rules do not require that such groups be made when there is a common technical feature, such as here where both measure ERK8 levels". This is not found persuasive because the technical feature is not special as exemplified in the Requirement mailed August 31, 2007 and the PCT rules are not applicable in the is U.S. filed case.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 1-20 are pending.

Claims 1-14, 19 and 20, drawn to non-elected inventions are withdrawn from examination.

Claims 15-18 are examined on the merits.

Priority

3. Acknowledgment is made of Applicant's claim for priority under 35 U.S.C. § 119(e). The Examiner has reviewed U.S. Provisional Application 60/478,992, filed June 17, 2003 from which priority is claimed. There seems to be no contemplation of a method of monitoring the effectiveness of an anti-cancer agent comprising assaying ERK8 levels disclosed in the provisional application. Thus, the claims will be granted

the priority date of the PCT international application (PCT/US04/19181) filed June 17, 2004.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 15-18 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The written description in this case only sets forth SEQ ID NO: 1 as a human extracellular signal-regulated kinase 8 (ERK8) polypeptide sequence, see page 4 of the Specification, lines 20-24.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116). Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 115).

Applicants are not required to disclose every species encompassed by a genus.

For example as indicated in *The Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

Applicants broadly claim a method of monitoring the effectiveness of anti-cancer agent comprising monitoring ERK8 levels, however ERK8 is not defined in the claims. Moreover, the specification notes the term "ERK8" refers not only to SEQ ID NO: 1, but fragments thereof, see page 8, lines 4 and 5. However, Applicants are not entitled, nor is the specification enabled for the method encompassing undefined proteins, variants for said an undefined and uncharacterized ERK8 polypeptide. Applicant is only in possession of one species of the ERK8 polypeptide, which is SEQ ID NO: 1. Applicants are not permitted to claim all extracellular signal-regulated kinase 8 that are encompassed by the claims, hence not entitled to the wide breadth of the claims at issue. There is no disclosure, beyond the mention of SEQ ID NO: 1 as an ERK8 polypeptide. And as Applicants' claims are written the recitation "ERK8" could encompass variants, mutants and proteins from not only humans, but other animals. There is no description of the sites at which variability may be tolerated and there is no information regarding the relation of structure to function. Structural features that could

distinguish the compounds in the genus from others excluded are missing from the disclosure.

This is insufficient to support the generic claims as provided by the Interim Written Description Guidelines published in the June 15, 1998 Federal Register at Volume 63, Number 114, pages 32639-32645.

Applicants can obviate the instant rejection my amending the claims to reflect that the ERK8 polypeptide of the claims reads specifically on SEQ ID NO: 1.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 15-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claim 15 is indefinite, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: a correlation step, which notes a certain level of ERK8 denotes treatment is or is not beneficial to the estrogen responsive cancers or the level of ERK8 corresponds, indicates positive or negative response to the anti-cancer agent.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

9. Claims 15, 16 and 18 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent number 6,759,221 (filed August 18, 2000/ IDS reference 1 submitted March 16, 2006). The patent discloses a protein kinase that shares sequence homology with Applicants' ERK8 polypeptide, see alignment below.

```
RESULT 1
US-09-641-690A-2
; Sequence 2, Application US/09641690A
; Patent No. 6759221
; GENERAL INFORMATION:
;  APPLICANT:  Hodge, Martin R.
;  TITLE OF INVENTION:  14189, A No. 6759221el Human Kinase and Uses
;  TITLE OF INVENTION:  Thereof
;  FILE REFERENCE:  5800-153
;  CURRENT APPLICATION NUMBER: US/09/641,690A
;  CURRENT FILING DATE:  2000-08-18
;  NUMBER OF SEQ ID NOS:  13
;  SOFTWARE:  FastSEQ for Windows Version 4.0
; SEQ ID NO 2
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;   LENGTH: 544
;   TYPE: PRT
;   ORGANISM: Homo sapiens
;   FEATURE:
;   NAME/KEY: VARIANT
;   LOCATION: (1)...(544)
;   OTHER INFORMATION: Xaa = Any Amino Acid
US-09-641-690A-2

  Query Match           98.4%;  Score 2483;  DB 2;  Length 544;
  Best Local Similarity  89.0%;  Pred. No. 1.3e-195;
  Matches  484;  Conservative    0;  Mismatches    0;  Indels   60;  Gaps    1;

Qy          1 MCTVVDPRIVRRYLLRRQLGQGAYGIVWKAVDRRTGEVVAIKKIFDAFRDKTDAQRTFRE 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MCTVVDPRIVRRYLLRRQLGQGAYGIVWKAVDRRTGEVVAIKKIFDAFRDKTDAQRTFRE 60

Qy         61 ITLLQEFGDHPNIISLLDVIRAENDRDIYLVFEFMDTDLNAVIRKGGLLQDVHVRSIFYQ 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 ITLLQEFGDHPNIISLLDVIRAENDRDIYLVFEFMDTDLNAVIRKGGLLQDVHVRSIFYQ 120

Qy        121 LLRATRFLHSGHVVHRDQKPSNVLLDANCTVKLCDFGLARSLGDLPEGPEDQAVTEYVA- 179
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 LLRATRFLHSGHVVHRDQKPSNVLLDANCTVKLCDFGLARSLGDLPEGPEDQAVTEYVAT 180

Qy        180 ------------------------------------------------------------E 180
                                                                           |
Db        181 RWYRAPEVLLSSHRYTLGVDMWSLGCILGEMLRGRPLFPGTSTXHQLELILETIPPPSEE 240

Qy        181 DLLALGSGCRASVLHQLGSRPRQTLDALLPPDTSPEALDLLRRLLVFAPDKRLSATQALQ 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 DLLALGSGCRASVLHQLGSRPRQTLDALLPPDTSPEALDLLRRLLVFAPDKRLSATQALQ 300

Qy        241 HPYVQRFHCPSDEWAREADVRPRAHEGVQLSVPEYRSRVYQMILECGGSSGTSREKGPEG 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 HPYVQRFHCPSDEWAREADVRPRAHEGVQLSVPEYRSRVYQMILECGGSSGTSREKGPEG 360

Qy        301 VSPSQAHLHKPRADPQLPSRTPVQGPRPRPQSSPGHDPAEHESPRAAKNVPRQNSAPLLQ 360
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 VSPSQAHLHKPRADPQLPSRTPVQGPRPRPQSSPGHDPAEHESPRAAKNVPRQNSAPLLQ 420

Qy        361 TALLGNGERPPGAKEAPPLTLSLVKPSGRGAAPSLTSQAAAQVANQALIRGDWNRGGGVR 420
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        421 TALLGNGERPPGAKEAPPLTLSLVKPSGRGAAPSLTSQAAAQVANQALIRGDWNRGGGVR 480

Qy        421 VASVQQVPPRLPPEARPGRRMFSTSALQGAQGGARALLGGYSQAYGTVCHSALGHLPLLE 480
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        481 VASVQQVPPRLPPEARPGRRMFSTSALQGAQGGARALLGGYSQAYGTVCHSALGHLPLLE 540

Qy        481 GHHV 484
              ||||
Db        541 GHHV 544
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The patent discloses "[m]onitoring the influence of agents (e.g., drugs, compounds) on the expression or activity of kinase genes (e.g., the ability to modulate aberrant cell proliferation and/or differentiation) can be applied not only in basic drug screening but also in clinical trials. For example, the effectiveness of an agent, as

determined by a screening assay as described herein, to increase or decrease kinase gene expression, protein levels, or protein activity, can be monitored in clinical trials of subjects exhibiting decreased or increased kinase gene expression, protein levels, or protein activity. In such clinical trials, kinase expression or activity and preferably that of other genes that have been implicated in for example, a cellular proliferation disorder, can be used as a marker of cellular growth and differentiation.", see column 9, line 57-column 10, lines 54; column 46, lines 26-40; column 45, lines 37-53; column 46, line 41-column 47, line 12.

"In another embodiment, modulators of kinase expression are identified in a method in which a cell is contacted with a candidate compound and the expression of kinase mRNA or protein in the cell is determined relative to expression of kinase mRNA or protein in a cell in the absence of the candidate compound.", see column 34, lines 42-47.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. Claims 15-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent number 6,759,221 (filed August 18, 2000/ IDS reference 1 submitted March 16, 2006), and further in view of Inoue et al. (Journal of Molecular Endocrinology 29:

175-192, 2002). The teachings of the patent have been presented in the 102(e) rejection. The patent does not teach the method wherein the estrogen responsive cancer cells contacted with the anti-cancer agent are from various established tumor cell lines.

However, Inoue teaches twelve cancer cell lines derived from breast, ovary and stomach that are estrogen responsive, see Abstract; page 176, bridging paragraph of columns 1 and 2, Cell culture section; and page 187, Estrogen-responsive section and corresponding Figure 6. It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the claimed invention was made to implement estrogen responsive cancer cells from various established tumor cell lines into the claimed method. One of ordinary skill in the art would have been motivated to implement the said cell lines in the claimed method with a reasonable expectation of success by the listed teachings because the patent does assess different cancer samples in order to determine the effectiveness of the candidate anti-cancer agent, see column 45, line 36-column 47, line 12.

12. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Alana M. Harris, Ph.D. whose telephone number is (571)272-0831. The examiner works a flexible schedule, however she can normally be reached between the hours of 7:30 am to 6:30 pm, with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Larry R. Helms, Ph.D. can be reached on (571) 272-0832. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

ALANA M. HARRIS, PH.D.
PRIMARY EXAMINER

Alana M. Harris, Ph.D.
12 January 2008